REMARKS

Claims 20 and 24-38 were pending in the subject application. The subject matter of Claims 24, 26 and 33-38 is allowable. By this amendment, applicants have canceled Claims 25 and 27-32 without prejudice or disclaimer, and have amended Claims 20, 24 and 26. Accordingly, upon entry of this Amendment, Claims 20, 24, 26 and 33-38 will be pending.

Applicants maintain that the amendments to the claims do not raise an issue of new matter. Claim 24 has been amended to be an independent claim which incorporates the features of previous Claim 20. Claim 26 has been amended to be an independent claim which incorporates the features of previous Claims 20 and 25. Support for the amendment to Claim 20 can be found in the specification at least on page 1, line 39 through page 2, line 1; page 7, lines 14-16; and page 10, lines 28-29. Accordingly, applicants respectfully request that the amendments be entered.

Summary of Attorney-Examiner Telephonic Interview

A telephonic interview was conducted on January 27, 2005 between Examiner Gailene R. Gabel and attorneys Craig Arnold and Alan Miller. Applicants thank the Examiner for the courtesy of the interview. The interview focused on differences between the present invention and the disclosure of Olsson et al., J. Appl. Biochem. 5:437-445, 1983, which has been cited against the subject invention under 35 U.S.C. §103(a), and on amendments that could be made to independent Claim 20. It was agreed that applicants would submit for the Examiner's further consideration a reply which includes the discussed claim amendments.

Applicants' attorneys concur with the Examiner's Interview Summary which is dated January 31, 2005.

Allowable Subject Matter

In the January 12, 2005 Office Action, the Examiner indicated that Claims 24, 26, and 33-38 would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Applicants have hereinabove rewritten Claims 24 and 26 in independent form. Accordingly, Claims 24, 26 and 33-38 should now be in condition for allowance.

Rejection of Claim 20 under 35 U.S.C. §103(a)

Claims 20 is rejected under 35 U.S.C. §103(a) as unpatentable over Olsson et al. (J. Appl. Biochem. 5:437-445, 1983) ("Olsson"), in view of Cruse et al. (Illustrated Dictionary of Immunology, 1995) ("Cruse").

Applicants respectfully traverse this rejection, and maintain that the claimed invention is patentable over the cited references as discussed below.

Olsson measured the accumulation of total adenylate kinase and hemoglobin in the plasma of preparations of red blood cells stored for as long as 41 days. Olsson described that there was a high degree of correlation between the amount of accumulated hemoglobin and adenylate kinase in the plasma of the stored units of red blood cells. Olsson's study was motivated by the need to evaluate the viability of stored erythrocytes and possible toxic effects due to the release of intracellular contents in blood stored in blood banks for use in blood transfusion. Olsson does not teach or suggest that erythrocyte adenylate kinase can be used as a marker for diagnosing

erythrocyte hemolysis *in vivo*.

Red blood cells contain a number of proteins including hemoglobin, acetylcholinesterase, adenylate kinase, aldolase, aspartate aminotransferase, creatine kinase, glucose-6-phosphate dehydrogenase, hexokinase, lactate dehydrogenase, malate dehydrogenase, phosphohexose isomerase, and pyruvate kinase (e.g., see Lindena et al., J. Clin. Chem. Clin Biochem. 24: 49-59 and 61-71, 1986, of record). The skilled artisan might consider any of the proteins contained within red blood cells as potential markers for hemolysis *in vivo* since a rupture of the red blood cells might release many of the proteins contained within the red blood cells. Nevertheless, not all red blood cell proteins are diagnostic for hemolysis *in vivo*. As discussed more fully in applicants' October 14, 2004 reply, the body's metabolism of red blood proteins is complex. By way of example, hemoglobin resulting from low levels of hemolysis is thought to form a complex with haptoglobin in plasma, which is subsequently removed by hepatic parenchymal cells. As such, hemoglobin cannot serve as a marker for low levels of hemolysis *in vivo*. In addition, plasma hemoglobin levels are normal in patients with most hereditary hemolytic anemias (Crosby et al. J Lab Clin Med 38:829-41: 1951, of record). Serum levels of lactate dehydrogenase, an intracellular component of red blood cells, are elevated in hemolysis, but may also be elevated in hepatic, cardiac, pulmonary, and placental diseases, thus reducing the test's specificity for detecting hemolysis. In addition, lactate dehydrogenase levels are inconsistently variable in conditions of extravascular hemolysis. The Examiner should appreciate that the natural clearance of blood proteins *in vivo* simply does not take place in a blood storage bag, and that not all red blood cells proteins are effective diagnostic markers for hemolysis *in vivo*.

Applicants note that Cruse et al. was cited by the Examiner only for the purpose of teaching a serum sample as an alternative to a plasma sample.

In view of the remarks and amendments made hereinabove, applicants submit that the invention set forth in Claim 20 is patentable over the cited references. Accordingly, reconsideration and withdrawal of this ground of rejection are respectfully requested.

CONCLUSIONS

In view of the amendments and remarks made herein above, reconsideration and withdrawal of the rejections in the January 12, 2005 Office Action and passage of the pending claims to allowance are respectfully requested. If there are any minor matters that prevent allowance of the subject application, the Examiner is requested to telephone the attorneys listed below.

No fee is deemed necessary in connection with the submission of this response. However, if any fee is required to maintain the pendency of the subject application, the Patent Office is authorized to withdraw the amount of any such fee from Deposit Account No. 01-1785.

Respectfully submitted,

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February 3, 2005

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